PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32528A/USN	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/06195	International filing date *(day/month/year)* 12.06.2003	Priority date *(day/month/year)* 13.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/405		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 03.12.2003	Date of completion of this report 28.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Fanni, S Telephone No. +49 89 2399-8712

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/06195

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 14

   because:

   ☒ the said international application, or the said claims Nos. 14 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,4,7,13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1,4,7,13
Industrial applicability (IA)	Yes:	Claims	1,4,7,13
	No:	Claims	

2. Citations and explanations

see separate sheet

ITEM III

Claim 14 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT). See also the paragraph on : "Industrial applicability" in item V below.

ITEM V

Reference is made to the following documents:

D1: US 354772
D2: EP 547000
D3: WO0236563

NOVELTY (Article 33(2) PCT)

The preset subject matter overlaps with D1 and D2, of which is considered to be a novel selection on account of the present calcium salt of formula IA.

The present subject matter differs from D3 on on account of the present calcium salt of formula IA.

INVENTIVE STEP (Article 33(3) PCT)

D1 is considered to be the closest prior art and discloses indole derivatives, including present compound of formula IB, as inhibitors of HMG-CoA reductase. Although pharmaceutical acceptable cations are claimed (cf claim 1, definition of M), only Sodium and Potassium salts are specifically disclosed (cf examples, e.g. example 6, 8, 9, 22 and 39).

D2 discloses pharmaceutical composition comprising, inter alia, present compound of formula IB and carbonate salts, including sodium and calcium carbonate. The said carbonate are said in D2 to be inert to compound of formula I according to D2 (i.e. present compound of formula IB); it appears therefore that D2 ruled out the formation of present compound of formula IA during the formation of pharmaceutical composition according to claim 1 of D2 (cf. page 3, lines 20-28).

D3 discloses crystalline forms of the sodium salts derivative disclosed in D1.

The Applicants appears to have set themselves the target of providing salt derivative of compound of formula IB which have an increased stability at pH about 8 or below when compared to the salts derivative of the same compounds known from the prior art.

Present compounds of formula IA are proposed as a solution for the given problem. Neither D2 nor D3 provide information which might suggest that the calcium salt of compound of formula IA according to D1 have improved properties when compared to the corresponding sodium salt. However, also the present application does not provide any data which would clearly show, in a comparative matter, that the present salts have unexpected properties when compared with the closest prior art compounds, i.e. unexpectedly solve a problem not yet solved.

Accordingly an inventive step cannot be acknowledged for the present subject matter.

INDUSTRIAL APPLICABILITY (Article 33(4) PCT)

For the assessment of the present claim 14 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.